REMARKS

The Examiner has rejected Claims 1 through 17. Claims 2 and 10 are canceled by way of the above amendment. Claims 1, 3 through 9, 11 through 17 are pending.

Independent claims 1 and 9 have been amended to specifically recite l-lactate salt within the solvent system. Claims 3, 4 and 11 have been amended to correct dependency in alignment with the above amendment. It is believed that no new matter has been added by way of the above amendment.

Rejection under 35 U.S.C. §112:

The Examiner rejected claims 1, 2, 4-6, 9, 10, 12-14 and 17 under 35 U.S.C. §112, first paragraph, because the specification does not provide an enabling disclosure for the scope of lactate salt. Specifically, the Examiner argues that the examples pertaining to l-lactate salt with acetaminophen would require undue experimentation to ascertain other lactate salts.

Applicants have amended independent claims 1 and 9 to limit the lactate salt element to l-lactate salts in accordance with the Examiner's position. The specification fully supports the claimed scope for this element, provides an enabling disclosure for such, and the specification contains an adequate written description for a skilled artisan to practice the invention without undue experimentation. Applicants have fully addressed the Examiner's concerns regarding the lactate salts. This rejection should, therefore, be withdrawn.

Rejections under 35 U.S.C. §103:

The Examiner rejected claims 1, 6, 9, 12 through 14, and 17 under 35 U.S.C. §103(a) as being unpatentable over Yu et al. U.S. Patent No. 5,071,643 in combination with Honour et al. U.S. Patent No. 5,529,923. Applicants respectfully traverse this

rejection for the following reasons.

The Examiner argues that Yu teaches a solvent system for acetaminophen comprising polyethylene glycol and hydroxide ions, water, glycerin and polyvinyl pyrrolidone for soft gel encapsulation. The Examiner states that Yu does not teach lactate salt. The Examiner relies on Honour for a "solution composition" with wetting agents such as sodium lactate. The Examiner concludes that one of ordinary skill in the art would have found the addition of "excipients" to "a solution of acetaminophen" to be obvious – alleging that one would have been motivated to do this to "maintain a solution at approximate physiological conditions".

At the onset, Applicants would like to re-introduce Applicants' invention. Difficulties have been encountered with balancing the solubility, concentration per fill volume, chemical compatibility with capsule material, and bioavailability of acetaminophen to accomplish encapsulated dosage forms containing the drug. The relevant overall context of the invention is, therefore, improved encapsulated dosage forms containing solubilized acetaminophen.

Applicants discussed the shortcomings of the Yu reference in the Background section of the specification on pages 2 to 3. Yu teaches solubilizing acetaminophen with hydroxide ions, polyethylene glycol and water. The problem associated with Yu, which is overcome by Applicants' invention, is the degradation of the capsular material by the levels of hydroxide ion source and its effect on the solution pH. The Examiner concedes that this reference fails to teach or suggest a lactate salt in the formulation.

Honour et al. is directed to pharmaceutical applications of a *flavobacterium* microbial strain. The text relied upon by the Examiner, column 8, lines 56 through 64, for a teaching of "lactate salts" actually pertains to *intravenous* compositions for

administration of the bacterium. The lactat salt is one of the "auxiliary substances" that can be included in the composition for approximating the "physiological conditions" of the blood. Clearly the Examiner has applied a reference that is not even technologically relevant to the field of Applicants' invention, i.e., capsular oral dosage forms containing solubilized acetaminophen. Certainly, one of ordinary skill would not have found the teachings of this reference to be technologically combinable with Yu et al. No rational motivation can be found to combine Yu et al. with Honour et al. to begin with – and the combination would not lead one of ordinary skill in the relevant art even remotely toward Applicants' invention. It is not understood by Applicants why one of ordinary skill would want to use a lactate salt to accommodate an intravenous administration environment in order to solubilize acetaminophen which is not even suggested in the Honour reference. This is technologically non-sensical. The Examiner applied an inappropriate level of hindsight as well as creativity to compile the rejection.

The Examiner has failed to present reference which, individually or in combination, fairly teach or suggest Applicants' invention. Accordingly, a combination of teachings which can adequately support a rejection on obviousness grounds has not been established.

Given the above references, the claimed invention is not unpatentable within the proper meaning of 35 U.S.C. §103(a). This rejection should, therefore, be withdrawn.

The Examiner rejected claims 2, 3, 10 and 11 under 35 U.S.C. §103(a) as being unpatentable over Yu et al. U.S. Patent No. 5,071,643 in combination with Honour et al. U.S. Patent No. 5,529,923 in combination with Veech U.S. Patent No. 6,020,007. Applicants respectfully traverse this rejection for the following reasons.

The Examiner argues that, in addition to the above arguments of the prior

obviousness rejection, that Veech teach s that the "l-form" of salts are preferred in "physiological conditions". Th Examiner then conclud s that the use of the "l-form" of lactate salt would have be n obvious and one of ordinary skill would have been motivated to do this to "maintain a solution that is suitable and preferred in the physiological environment to which it is administered".

The shortcomings of Yu and Honour have been discussed in Applicants' remarks to the above rejection under 35 U.S.C. §103(a) and are likewise applicable here and repeated herein. The Examiner relies upon Veech for a teaching of l-lactate.

Veech pertains to *electrolyte solutions* and fluid therapy. Again, the Examiner has pulled a compound out of a technologically irrelevant reference and context. In column 2 of the Veech reference, the relevant context of the Veech invention is described, i.e., orally ingested aqueous solutions, parenteral (intravenous) therapy, dialysis, and irrigation therapy. There is no mention of acetaminophen and l-lactate within encapsulated dosage forms. The reference does not even have to do with fill formulations for capsular dosage forms.

So now the Examiner has in effect alleged that one of ordinary would have combined an ingredient of an electrolyte solution for fluid therapy together with an intravenous auxiliary substance for bacteria and with an oral encapsulated solubilized acetaminophen composition to arrive at Applicants' invention. Of course, these references are not properly combinable to one of ordinary skill because they are not even technologically related to the field of Applicants' invention. Logically, there can be non rational or scientifically sound motivation to assemble these references to arrive at the claimed invention. The Examiner applied an inappropriate level of hindsight and creativity to compile the rejection.

Given the above references, the claimed invention is not unpatentable within the proper meaning of 35 U.S.C. §103(a). This rejection should, therefore, be withdrawn.

The Examiner rejected claims 4, 5, 7, 8, 12, 13, 15 and 16 under 35 U.S.C. §103(a) as being unpatentable over Yu et al. U.S. Patent No. 5,071,643 in combination with Honour et al. U.S. Patent No. 5,529,923 in combination with Veech U.S. Patent No. 6,020,007 in combination with Shelley et al. U.S. Patent No. 5,505,961. Applicants respectfully traverse this rejection for the following reasons.

The Examiner argues that, in addition to the above arguments of the previous obviousness rejection, Shelley teaches that "potassium acetate aids in the solubility of acetaminophen". The Examiner concludes that one of ordinary skill in the art would have found the incorporation of potassium acetate into a solvent system for acetaminophen to be obvious and one would have been motivated to do so to aid in the solubility of acetaminophen.

The shortcomings of Yu, Honour and Veech have been discussed in Applicants' remarks to the above rejection under 35 U.S.C. §103(a) and are likewise applicable here and repeated herein.

The shortcomings of Shelley et al. are discussed in the Background section of Applicants' specification on page 3. Specifically, the examiner relies upon Shelley et al. for a teaching of potassium acetate for solubilizing acetaminophen.

Again as with Yu et al., Applicants' discussed the disadvantages of Shelley et al. in the Background section of the specification on page 3. As stated therein, the problem is that while solubilizing desired amounts of acetaminophen the fill volume is relatively large. It is this problem that Applicants' invention addresses and overcomes. In other words, Applicants' instant invention is an *improvement* of systems such as those

d scribed in Shelley et al. This improvement is qualified with experimental data on pages 10 through 13, wherein Applicants' have surprisingly struck a balance that maintains desirable attributes of the fill formulation for encapsulation. Shelley et al. does not teach or suggest l-lactate salts within the solvent system for acetaminophen. The two technologically relevant references applied by the Examiner, i.e., Yu et al. and Shelley et al., even when combined, still do not arrive at the combination of acetaminophen with l-lactate salts. In addition to the inadequacy of the teachings of Yu et al. and Shelley et al. per se, the motivation to combine l-lactate salts with acetaminophen for capsular fill compositions is still absent. The Examiner's alleged motivation could only have arisen from improper levels of hindsight and creativity.

Given the above references, the claimed invention is not unpatentable within the proper meaning of 35 U.S.C. §103(a). This rejection should, therefore, be withdrawn.

Conclusion:

In light of the above amendments and the accompanying remarks, it is believed that the application is now in condition for allowance, and prompt notification to that effect is earnestly solicited. The Examiner is invited to contact the undersigned to discuss the application on the merits if it is believed that such discussion would expedite the prosecution.

Respectfully submitted,

Dated: Dec. 9, 2003

Andrew G. Rozycki, Reg. No. 36,406
Attorney for Applicants
Cardinal Health, Inc.
7000 Cardinal Place
Dublin, Ohio 43017
Tel. (614) 757-7413
Fax (614) 757-2243